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Dialog level 00.03.29D

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                    *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
  5.  Product Descriptions

 Connections:
  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)
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     /H = Help            /L = Logoff          /NOMENU = Command Mode


Enter an option number to view information or to connect to an online
 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
?B 352

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     $0.00  Estimated cost FileHomeBase
            KMKNET2   0.004 Hrs.
     $0.00  Estimated cost this search
     $0.00  Estimated total session cost   0.147 DialUnits

File 352:DERWENT WPI  1963-2000/UD=, UM=, & UP=200019
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*File 352: Display format changes coming soon.  Try them out
now in ONTAP File 280.  See HELP NEWS 280 for details.

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 1/7/1
DIALOG(R)File 352:DERWENT WPI
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004823542
WPI Acc No: 86-326883/198650
  Process for amplifying detecting or cloning nucleic acid sequences -
  useful in disease diagnosis and in prepn. of transforming vectors
Patent Assignee: CETUS CORP (CETU  ); HOFFMANN LA ROCHE F (HOFF  );
  HOFFMANN LA ROCHE & CO AG F (HOFF  )
Inventor: ARNHEIM N; ERLICH H A; HORN G T; MULLIS K B; SAIKI R K; SCHARF S
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Number of Countries: 019 Number of Patents: 031

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 200362	A	19861210	EP 86302298	A	19860327		198650 B
AU 8655322	A	19861002					198652
AU 8655323	A	19861002					198652
JP 61274697	A	19861204	JP 8668858	A	19860328		198703
JP 62000281	A	19870106	JP 8668857	A	19860328		198706
DK 8601448	A	19860929					198731
DK 8601449	A	19860929					198731
US 4683195	A	19870728	US 85791308	A	19851025		198732
US 4683202	A	19870728	US 86828144	A	19860207		198732
ES 8706822	A	19870916	ES 553464	A	19860326		198741
ES 8706823	A	19870916	ES 553468	A	19860326		198741
ZA 8602334	A	19870928	ZA 862334	A	19860327		198751
ZA 8602335	A	19870928	ZA 862335	A	19860327		198751
ES 8800356	A	19880101	ES 87557287	A	19870109		198809
ES 8800357	A	19880101	ES 87557288	A	19870109		198809
CA 1237685	A	19880607					198827
US 4800159	A	19890124	US 86943948	A	19861217		198906
US 4683195	B	19901127					199050 N
US 4683202	B	19901127					199050
IL 78281	A	19910610					199130
CA 1291429	C	19911029					199151
IL 78284	A	19910916					199205
JP 92067957	B	19921029	JP 8668857	A	19860328	C12N-015/10	199248
JP 92067960	B	19921029	JP 8668858	A	19860328	C12Q-001/68	199248
EP 200362	B1	19930120	EP 86302298	A	19860327	C12Q-001/68	199303
DE 3687537	G	19930304	DE 3687537	A	19860327	C12Q-001/68	199310
			EP 86302298	A	19860327		
JP 6007166	A	19940118	JP 8668858	A	19860328	C12N-015/10	199407
			JP 92177761	A	19860328		
DK 171160	B	19960708	DK 861448	A	19860326	C12P-019/34	199633
DK 171161	B	19960708	DK 861449	A	19860326	C12Q-001/68	199633
JP 2546576	B2	19961023	JP 8668858	A	19860328	C12N-015/09	199647
			JP 92177761	A	19860328		
CA 1340121	E	19981110	CA 617031	A	19951026	C07H-021/00	199904 N

Priority Applications (No Type Date): US 86828144 A 19860207; US 85716975 A 19850328; US 85791308 A 19851025; US 86824044 A 19860130; CA 617031 A 19951026

Cited Patents: 2.Jnl.Ref; A3...8708; EP 138242; EP 139501; EP 155188; EP 86548; No-SR.Pub; US 4351901

Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
EP 200362	A	E	46			
Designated States (Regional): AT BE CH DE FR GB IT LI LU NL SE						
JP 92067957 B			29	Based on		JP 62000281
JP 92067960 B			36	Based on		JP 61274697
EP 200362	B1	E	51			
Designated States (Regional): AT BE CH DE FR GB IT LI LU NL SE						
DE 3687537	G			Based on		EP 200362
JP 6007166	A		40	Div ex	JP 8668858	
DK 171160	B			Previous Publ.		DK 8601448
DK 171161	B			Previous Publ.		DK 8601449
JP 2546576	B2		36	Div ex	JP 8668858	
				Previous Publ.		JP 6007166
CA 1340121	E			Reissue of		CA 1291429

Abstract (Basic): EP 200362 A

The novelty comprises a process for amplifying and detecting any target nucleic acid sequence (I) contd. in a nucleic acid or mixt. and for distinguishing between two different sequences in a nucleic acid. The process comprises treating separate complementary strands of the nucleic acid with a molar excess of two oligonucleotide primers, extending the primers to form complementary primer extension prods

which act as templates for synthesising (I), and detecting (I) so amplified. In an embodiment (also claimed), the synthesis of (I) is effected opt. in the presence of DMSO or at up to 45 deg.C. restriction enzymes are added for each of restriction sites present on the 5' end of the primers used, and after cleavage, the prod. is ligated into a cloning vector. The process may also be used (claimed) to synthesise a nucleic acid fragment from an existing nucleic acid fragment (II) having fewer nucleotides than the fragment being synthesised and two oligonucleotide primers. The prod. comprises a core segment, which is (II), and right and left segments representing the nucleotide sequence present in the 5' ends of the two primers, the 3' ends of which are complementary to the 3' ends of the single strands produced by sepg. the strands of (II).

USES/ADVANTAGES - The method may be used to detect (I) associated with infectious diseases, genetic disorders or cellular disorders such as cancer, e.g. oncogenes. The amplification is advantageous when the amt. of nucleic acid available is small, e.g. in the prenatal diagnosis of sickle cell anaemia using DNA obtd. from foetal cells. In addn., the method may be utilised to clone a particular nucleic acid sequence for insertion into an expression vector. The vector may then be used to transform a host to produce the gene prod. of the sequence by standard methods of recombinant DNA technology

Dwg.0/10

Abstract (Equivalent): EP 201184 B

A process for exponentially amplifying at least one specific, double-stranded nucleic acid sequence contained in a nucleic acid or a mixture of nucleic acids wherein each nucleic acid consists of two complementary strands, of equal or unequal length, which process comprises: (a) treating the strands with a molar excess of two oligonucleotide primers, one for each of the strands, under hybridising conditions and in the presence of an inducing agent for polymerisation and the different nucleotides, such that for each strand an extension product of the respective primer is synthesised which is complementary to the nucleic acid strand, wherein said primers are selected so that each is substantially complementary to one end of the sequence to be amplified on one of the strands such that an extension product can be synthesised from one primer which, when it is separated from its complement, can serve as a template for synthesis of an extension product of the other primer; (b) separating the primer extension products from the templates on which they were synthesised to produce single-stranded molecules; (c) treating the single-stranded molecules generated from step (b) with the primers of step (a) under hybridising conditions and in the presence of an inducing agent for polymerisation and the different nucleotides such that a primer extension product is synthesised using each of the single-strands produced in step (b) as a template; and, if desired, (d) repeating steps (b) and (c) at least once; whereby the amount of the sequence to be amplified increases exponentially relative to the number of steps in which primer extension products are synthesised.

Dwg.0/10

EP 200362 B

A process for detecting the presence or absence of at least one specific double-stranded nucleic acid sequence in a sample, or distinguishing between two different double-stranded nucleic acid sequences in said sample, which process comprises first exponentially amplifying the specific sequence or sequences (if present) by the following steps, and then detecting the thus-amplified sequence or sequences (if present): (a) separating the nucleic acid strands in the sample and treating the sample with a molar excess of a pair of oligonucleotide primers for each different specific sequence being detected, one primer for each strand, under hybridising conditions and in the presence of an inducing agent for polymerisation and the different nucleoside triphosphates such that for each of said strands an extension product of the respective primer is synthesised which is complementary to the strand, wherein said primers are selected so that each is substantially complementary to one end of the sequence to be amplified on one of the strands such that the extension product

synthesized from one primer, when it is separated from its complement, can serve as a template for synthesis of an extension product of the other primer of the pair; (b) treating the sample resulting from (a) under denaturing conditions to separate the primer extension products from their templates; (c) treating as in (a) the sample resulting from (b) with oligonucleotide primers such that a primer extension product is synthesised using each of the single strands produced in step (b) as a template; and, if desired, (d) repeating steps (b) and (c) at least once; whereby exponential amplification of the nucleic acid sequence or sequences, if present, results thus permitting detection thereof; and, if desired, (e) adding to the product of step (c) or (d) a labelled oligonucleotide probe capable of hybridising to said sequence to be detected; and (f) determining whether said hybridisation has occurred.

Dwg.0/10

Abstract (Equivalent): US 4800159 A

Specific nucleic acid sequence contd. in a nucleic acid (mixt.) a cloned into a rector, by (a) treating nucleic acid(s) with a oligonucleotide primer per strand of each different specific suequence to be amplified such that an extension prod. of each primer is synthesised so as to be complementary to each strand of sequence to be hybridised, such that when extension prod. is sepd. from its complement, it can act as a template for synthesis of the extension prod. of the other primer. Each primer contains a restrictive site on its S'end which is opt. different from those of the other primer(s).

Process then comprises (b) sepg. primer extension prods. from the templates upon which they were synthesised to form single stranded molecules; (c) treating these with oligonucleotide primers so that a primer extension prod. is formed using each single strand as template, opt. using 0-10% dimethylsulphoxide and temp. of 35-45 deg.C in (a) and/or (c) as necessary: (d) adding prod. a restriction enzyme for each resiction site to form cleaved prods. in a restriction digest: and (e) ligating cleaved prod(s) into cloning rector(s).

USE - For amplifying nucleic acid sequence of or contained in beta-clobin gene or N-RAS oncogene.

US 4683202 A

At least 1 specific nucleic acid (NA) sequence contained in a NA (mixt.) where each NA consists of 2 separate complimentary strands of (un)equal length, is amplified by (A) treating the strands with 2 oligonucleotide primers for each sequence to synthesise extension products of each primer complimentary to each NA strand; sufficiently different primers are used so that the extension product when sepd. from its complement can be used as template for the synthesis of the extension product of the other primer; (B) sepg. the extension products from the templates used for the synthesis and (C) treating the single stranded molecules obtd. with the above primers to synthesise primer extension products using the single strands obtd. in (B) as a template.

Steps (B) and (C) are pref. repeated at least once. Step (B) is effected by denaturing, esp. by heating or using the enzyme helicase. Steps (A) and (C) are effected using an enzyme, esp. e.g. E coli DNA polymerase, reverse transcriptase where the template is RNA on DNA and the extension product is DNA. The NA is (a) DNA and the primers are oligodeoxyribonucleotides or (b) messenger RNA. The strands of the DNA are sepd. by physical, chemical or enzymatic means.

USE/ADVANTAGE - A more effective method than known ones to produce large amts. of NA avoiding propagation of any organisms or synthesis of unrelated NA sequences, cheaper equipment is used.

US 4683195 A

Process for detecting the pesence or absence of at least one specific nuclei acid sequence in a sample contg. a (mixt.) of nucleic acid) or distinguishing between two different sequences in the sample, comprises: (a) treating the sample with one oligonucleotide primer for each strand of each different specific sequence, under hybridising conditions such that for each strand of each different sequence to which an oligonucleotide primer is hybridized an extension prod. of each primer is synthesised which is complementary to each nucleic acid strand. The primer(s) are selected to be sufficiently complementary to

each strand of each specific seqeunce to hybridge therewith such that the extension prod. synthesised from one primer, when it is sepd. from its complement, can serve as a template for synthesis of the extension prod. of the other primer; (b) treating the sample under denaturing conditions to separate the primer extension prods. from their templates if sequences to be detected are present; (c) treating the sample with oligonucleotide primers so that a primer extension prod. is synthesised using each of the single strands produced in step (v) as a template, resulting in amplification of the specific nucleic acid sequence(s) if present. (d) adding to the prod. of (c) a labelled oligonucleotide probe for each sequence being detected capable of hybridising to the sequence or a mutation thereof; and (e) determining whether hybridisation has occurred.

Derwent Class: B04; D16
International Patent Class (Main): C12N-015/09; C12P-019/34
International Patent Class (Additional): C07H-021/00; C07H-021/02; C07H-021/04; C12N-001/00; C12N-015/00; C12N-015/10; C12N-019/00; C12Q-001/68; G01N-033/53

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